REMARKS/ARGUMENTS

Favorable consideration of this application as presently amended and in light of the following discussion is respectfully requested.

Claims 1-19 are pending in the application, with Claims 1-15 having been amended by way of the present amendment and with Claims 16-19 withdrawn from consideration.

In the outstanding Office Action, Claims 1-15 were rejected under 35 U.S.C. § 112, second paragraph; Claims 1-2, 5, 7-9, 11 and 13-15 were rejected under 35 U.S.C. § 102(b) as being anticipated by Krihak et al. (U.S. Patent No.5,810,989, hereinafter Krihak); Claims 1-3, 5-8 and 11-15 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wang et al. (U.S. Patent No. 6,468,757, hereinafter Wang) in view of Brennan et al. (U.S. Patent No. 5,474,796, hereinafter Brennan); and Claims 4 and 9-10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wang in view of Brennan and further in view of Ohakwa (U.S. Patent No. 5,486,337).

Claims 1-15 have been amended to positively recite method steps and to more clearly describe and distinctly claim Applicants' invention. No new matter is added. Thus, Applicants submit the rejections under 35 U.S.C. § 112, second paragraph, have been overcome.

Briefly recapitulating, amended Claim 1 is directed to a method for producing a matrix, comprising dispensing with an electrode a ligand on one of a conductive carrier and a conductive zone of a carrier; and electrochemically fixing the ligand by the electrode to the one of a conductive carrier and a conductive zone of a carrier. In the invention, the ligand is coupled to an electropolymerisable monomer, and the step of electrochemical fixing by the electrode is performed via an electrically assisted synthesis of the electropolymerisable monomer coupled to the ligand. Also, the steps of dispensing and electrochemically fixing are conducted simultaneously. The ligand dispensing and fixing method recited in Claim 1

requires use of less reaction medium than conventional methods and therefore economizes the molecules of biological interest. Also, with the claimed invention the size of the droplets made on the carrier may be adjusted whereas in conventional mechanical methods droplet sizes cannot be less than 50-100 μm.[1]

Krihak teaches a method for synthesizing DNA probe arrays on a support, in which the DNA probes are formed by electropolymerization of oligonucleotide modified monomers. However, in the method of Krihak the support on which the DNA probes are synthesized comprises an insulating substrate 12 which is coated on one of its surfaces with an electrical conductive layer 14 that is coupled with a first lead 18 and that is itself coated with a photoconductive layer 16.[2] The support is immersed in a solution which contains the oligonucleotide modified monomers and which is also coupled with a second lead 20 so that a potential may be applied across leads 18 and 20 and thus between the electrical conductive layer 14 and the solution 22.[3] Also the electropolymerization of the oligonucleotide modified monomers is achieved by applying one or more beams of light, not via an electrode as recited in Applicants' Claim 1, through portions of the photoconductive layer 16 to complete an electrical circuit between the electrical conductive layer 14 and the solution 22.[4]

Thus, the method of Krihak firstly differs from the method of the invention in that the deposition of the solution containing the oligonucleotide monomers on the support and the electropolymerization of these monomers are carried out in two successive steps and not simultaneously. This is due to the fact that, in the method of Krihak, the solution containing the oligonucleotide modified monomers is not deposited on the support by a specific element, such as Applicants' claimed electrode, but simply by immersing the support in the solution. Thus, in the method of Krihak, the solution is not deposited only on the sites of the support

[1] Specification, page 14, line 17 – page 14, line 25.
[2] Krihak, Figure 2.
[3] Krihak, column 3, lines 6-7.
[4] Krihak, column 3, lines 48-52.

where DNA probes have to be synthesized, but on all the surface of the support, which is very expensive in nucleotides and monomers. This means that the method of Krihak does not allow to carry out a simultaneous synthesis of DNA probes of different types unlike to the method of the invention. Applicants note that Krihak teaches that the solution may also be applied on the surface of the support[5] but Krihak neither gives any detail concerning the means to be used for carrying out such an application, nor shows such a means. Therefore, Applicants submit Krihak does not teach Applicants' claimed method of dispensing.

The method of Krihak also differs from Applicants' claimed method in that Krihak's electropolymerization of the monomers is not carried out by means of an electrode but by means of one or more beams of light, notably visible laser beams. As a result, the method of by Krihak is more difficult to implement than Applicants' claimed method since Krihak requires not only means for providing one or more beams of light, but also the use of a support comprising both an electrical conductive layer and a photoconductive layer, as well as the use of masks for limiting the application of said beam(s) to the sites where DNA probes are to be synthesized.

At least because Krihak does not teach or suggest either a method including either dispensing or electrochemically fixing with an electrode, let alone simultaneous dispensing and fixing with an electrode, Applicants submit the inventions defined by Claim 1, and all claims depending therefrom, are not anticipated by Krihak.[6]

Regarding the Wang reference, Applicants note that the patent to Wang was granted on October 22, 2002 on the basis of an application filed on February 18, 2000 and claiming the benefit from a provisional application filed on February 19, 1999. However, Applicants' application claims priority to the French patent application 99-01438 which was filed on

[5] Krihak, column 3, lines 6-7.
[6] MPEP § 2142 "...the prior art reference (or references when combined) must teach or suggest **all** the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

February 8, 1999, 11 days before the date of filing of the Wang provisional application. Therefore, Applicants submit that the Wang patent is not prior art and cannot form a proper basis for rejection of Applicants' claimed invention. A certified translation of Applicants' priority application is filed herewith.

Applicants also submit that the method of Claim 1 is neither anticipated nor rendered obvious by the teachings of Wang. In the method of Wang, a test electrode 1 is put into contact with a solution 2 containing the DNA sequences to be detected.[7] A Ag/AgCl reference electrode 3 is also used to establish a working potential.[8] Current changes in the test electrode 1 relative to a reference electrode 3 are measured knowing that a current change occurs when a hybridization occurs between the free oligomer coupled to the conductive polymer and a DNA sequence present in the sample. The coating of the test electrode 1 with the conductive polymer film may be carried out by electrochemical deposition, notably by a cyclic voltametric deposition.[9]

However, Wang also teaches such a deposition is achieved by immersing the electrode either (1) in a solution containing the monomer and the oligomer, in which case the monomer is electropolymerized (thus the polymer film is formed while immersing the electrode in the solution); or (2) in a solution containing the polymer already formed together with the oligomer, in which case the monomer is electropolymerized before immersing the electrode in the solution.[10] Wang does not teach or suggest dispensing with an electrode or electrochemically fixing with an electrode, let alone simultaneously dispensing and electrochemically fixing with an electrode, as recited in Applicants' Claim 1.

Brennan teaches methods for making a matrix of ligands, such as peptides or oligonucleotides, fixed on the surface of a support. In these methods, a support having

[7] Wang, column 13, lines 36-47; Figure 1.
[8] Wang, column 14, lines 2-7; Figure 1.
[9] Wang, column 3, lines 63-67.
[10] Wang, column 8, lines 30-43.

hydrophilic binding sites is firstly prepared and then the ligands are deposited on these hydrophilic binding sites. Typically, the support having hydrophilic binding sites is a glass plate (that is to say an insulating support) having hydroxy- or aminosilane sites as hydrophilic binding sites. This support is prepared by a process consisting of: (1) coating the surface of the support with a positive or negative photoresist substance which is subsequently exposed and developed to create a patterned region of a first exposed surface of the support; (2) reacting the first surface of the support with a fluoroalkylsilane to form a stable fluoroalkylsiloxane hydrophobic matrix on the first surface of the support; (3) removing the remaining photoresist to expose a second surface of the support; and (4) reacting the second surface of the support with a hydroxy- or aminoalkylsilane to form derivatized hydrophilic binding sites.[11] The support of Brennan is not equivalent to Applicants' claimed conductive carrier or conductive zone of a carrier.

Furthermore, in Brennan, the deposition of the ligands on the hydrophilic binding sites of the support is carried out by means of a piezoelectric pump,[12] not via an electrode as recited in Applicants' Claim 1. This pump deposits microdroplets on the hydrophilic binding sites and the fixation of the ligands to these sites occurs by the formation of covalent bands between the ligands and the sites, or by the formation of non-covalent specific binding reactions such as an antibody/antigen binding reaction between the ligands and the sites. Furthermore, in the method of Brennan does not teach fixing the ligands to the carrier by electropolymerization of a monomer as recited in Applicants' Claim 1. Thus, Brennan does not cure the deficiencies of Wang.

Applicants therefore submit the outstanding rejection of Claim 1 in view of Wang and Brennan does not meet the burden of proving unpatentability as neither of these references, individually or in combination, disclose or suggest all the elements of independent Claim 1.

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[11] Brennan, column 2, line 29 – column 3, line 3.
[12] Brennan, column 8, lines 25-56.

Applicants have also considered the Ohkawa reference. Ohkawa teaches a method for manipulating nanovolume sized droplets of a liquid on the surface of a support (i.e., moving these droplets from one point of the support to another, by electrostatic forces) and therefore teaches against Applicants' method of fixing ligands on a support. In particular, the dispensing of the droplets to the support may be done by direct application of the liquid in bulk, by spray or by a portable dispensing implement such as an electrostatic pipette.[13] However, Ohkawa does not teach or suggest using this pipette for (a) depositing a ligand coupled to an electropolymerizable monomer on the support, or (b) electropolymerizing the monomer in order to fix a ligand to the support. Thus, Ohkawa does not cure the deficiencies of Wang and Brennan. Therefore, Applicants submit the inventions defined by Claim 1, and all claims depending therefrom, are not rendered obvious by the asserted prior art for at least the reasons stated above.[14]

Accordingly, in view of the present amendment and in light of the previous discussion, Applicants respectfully submit that the present application is in condition for allowance and respectfully request an early and favorable action to that effect.

Respectfully submitted,

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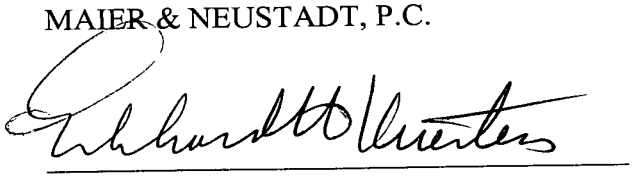

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[13] Ohkawa, column 7, lines 8-11; Figure 4.
[14] MPEP § 2142 "...the prior art reference (or references when combined) must teach or suggest **all** the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

Claim 1 (Currently Amended): ~~Method~~ A method for producing a matrix, comprising:

dispensing with an electrode a ligand on one of a conductive carrier and a conductive zone of a carrier; and

electrochemically fixing by the electrode the ~~at least one~~ ligand ~~fixed by electrochemical route~~ to ~~a~~ the one of a conductive carrier ~~or to~~ and a conductive ~~zones~~ zone of a carrier, wherein

the ligand ~~in which at least one element is used able to dispense the ligand(s)~~ is coupled to an electropolymerisable monomer, ~~as~~

the electrochemical fixing comprises an electrically assisted synthesis of the electropolymerisable monomer coupled to the ligand, and

~~electrode to carry out electrically assisted synthesis of a polymer carrying the ligand(s) on the conductive carrier or on the conductive zones of the carrier~~

the steps of dispensing and electrochemically fixing are conducted simultaneously.

Claim 2 (Currently Amended): ~~Method~~ The method according to claim 1, wherein the step of dispensing with an electrode comprises:

dispensing the ligand with an electrode having ~~in which said element is made up of~~ a reservoir containing the ligand coupled to electropolymerisable monomer and having a conductive part.

Claim 3 (Currently Amended): ~~Method~~ The method according to claim 2, wherein the step of dispensing with an electrode having a reservoir and conductive part comprises:

~~in which the~~dispensing with an electrode having a reservoir ~~is~~ provided with a ligand insertion and evacuation ~~means~~device.

Claim 4 (Currently Amended): ~~Method~~ The method according to claim 1, wherein the dispensing with an electrode comprises:

dispensing with one ~~in which said element is made up~~ of ~~an~~ a wire electrode ~~in wire~~ and a ~~or~~ needle ~~form~~electrode, wherein

the one of a wire electrode and a needle electrode is charged externally ~~with ligand coupled to the electropolymerizable monomer~~, and

~~the~~ a contact is established between the one of a wire electrode and a needle electrode and the one of a conductive carrier ~~or~~ and a conductive zone of ~~the~~ a carrier ~~being assured during the fixing operation~~ by ~~means of~~ a drop of ligand ~~withheld by~~on the electrode.

Claim 5 (Currently Amended): ~~Method~~ The method according to claim 1~~any of claims 1 to 4~~, further comprising:

dispensing with the electrode another ligand on another one of a conductive carrier and a conductive zone of a carrier; and

electrochemically fixing the another ligand to the another one of a conductive carrier and a conductive zone of a carrier, wherein

the steps of dispensing and electrochemically fixing the another ligand are conducted simultaneously, and

the steps of dispensing with an electrode and dispensing with a second electrode are conducted either simultaneously or successively.~~in which identical or different ligands are~~

~~fixed simultaneously or successively on different conductive sites of the carrier by using several elements respectively dispensing identical or different ligands.~~

Claim 6 (Currently Amended): ~~Method~~ The method according to claim 5, wherein the steps of dispensing with an electrode and dispensing with a second electrode comprise:

dispensing ~~in which at least two of the elements are grouped together to form~~with a print head including the electrode and the second electrode.

Claim 7 (Currently Amended): The method ~~Method~~ according to claim 1, ~~any of claims 1 to 4,~~ further comprising:

dispensing with the electrode another ligand on another one of a conductive carrier and a conductive zone of a carrier; and

electrochemically fixing the another ligand to the another one of a conductive carrier and a conductive zone of a carrier, wherein

the steps of dispensing with an electrode, dispensing with a second electrode, electrochemically fixing the ligand, and electrochemically fixing the at least one other ligand are conducted simultaneously ~~in which at least two different ligands are successively fixed to different sites of the carrier using a single element and by changing at least once the ligand dispensed by this element~~.

Claim 8 (Currently Amended): The method ~~Method~~ according to claim 1~~any of claims 1 to 4~~, wherein the step of dispensing comprises:

dispensing ~~the~~a ligand on a plurality of conductive zones ~~in which the conductive zones are~~ formed of zones of conductive material arranged on an insulating carrier.

Claim 9 (Currently Amended): The method ~~Method~~ according to claim 8, wherein the step of dispensing a ligand on a plurality of conductive zones comprises:

~~in which~~ dispensing a ligand on ~~the~~ zones of conductive material which are electrically interconnected.

Claim 10 (Currently Amended): The method ~~Method~~ according to claim 8, wherein the step of dispensing a ligand on a plurality of conductive zones comprises:

dispensing a ligand on ~~in which the~~ zones of conductive material which are electrically addressable either separately or in groups ~~so that they~~ which can be activated separately.

Claim 11 (Currently Amended): The method ~~Method~~ according to claim 8~~any of claims 8 to 10~~, wherein the step of dispensing a ligand on a plurality of conductive zones comprises:

~~in which the~~ dispensing the ligand on a conductive material ~~is~~ chosen from the group made up of gold, silver, platinum, indium and tin oxide (ITO), carbon, and conductive organic polymers.

Claim 12 (Currently Amended): The method ~~Method~~ according to claim 1, wherein the step of dispensing comprises:

dispensing~~in which each element dispenses~~ a solution ~~of ligand~~ containing the ~~ligand~~ligand coupled to ~~an~~ the electropolymerisable monomer~~, the electropolymerisable monomer and optionally~~ and a doping agent.

Claim 13 (Currently Amended): The method ~~Method~~ according to claim 1 ~~or 12~~, wherein the electropolymerisable monomer comprises:

~~in which the electropolymerisable monomer is~~ pyrrole.

Claim 14 (Currently Amended): The method ~~Method~~ according to claim 1 ~~or 13~~, wherein the step of electrochemically fixing the ligand comprises:

~~in which~~ fixing ~~of~~ the ligand ~~is obtained~~ by electro-copolymerisation of both the electropolymerisable monomer and ~~of~~ the ligand coupled to the electropolymerisable monomer.

Claim 15 (Currently Amended): The method ~~Method~~ according to claim 1 ~~any of claims 1 to 14~~, wherein the ligand comprises:

~~in which the ligand is~~ one of a nucleotide, an oligonucleotide, an amino acid, and ~~or~~ a peptide.

Claim 16 (Withdrawn): Device for producing a matrix of ligands on a conductive carrier or on conductive zones of a carrier, comprising:

- at least one ligand dispensing means (1) provided with a conductive part (3),

- means for connecting firstly the conductive carrier (7) or conductive zones (13) of the carrier, and secondly the conductive part (3) of the dispensing means to an electric generator, and

- means for positioning and/or moving the carrier and/or the dispenser means relative to one another and to place them in contact such as to carry out several ligand deposits on the carrier at different sites.

Claim 17 (Withdrawn): Device according to claim 16, in which said dispensing means comprises a reservoir (1) containing the ligand and at least one electrode (3, 5) arranged in said reservoir and forming the conductive part of said means.

Claim 18 (Withdrawn): Device according to claim 17, which comprises several ligand dispensing means assembled in the form of a print head.

Claim 19 (Withdrawn): Device for producing a matrix of ligands on a conductive carrier or on conductive zones of a carrier, comprising:

- an electrode (15) in wire or needle form able to be charged externally with said ligand,

- means for connecting firstly the conductive carrier (7) or conductive zones (13) of the carrier, and secondly the electrode (15) to an electric generator, and

- means for positioning and/or moving the carrier and/or electrode (15) relative to one another such as to carry out several ligand deposits on the carrier at different sites.